c29 cont'd

SCF(D124A, (SEQ ID NO:20); K127D (SEQ ID NO:21)).

Remarks

Claims 1-47 are currently pending in the subject application. After entry of this Amendment claims 1-47 will be pending. The January 18, 2002 Office Communication Concerning Non-Compliance with Sequence Compliance Rules issued by the United States Patent and Trademark Office in connection with the above-identified application indicates that the Amendment filed by applicant in response to an August 2, 2001 Office Communication was incomplete. Applicants attach hereto a copy of the Communication as **Exhibit A.** Specifically, the January 18, 2002 Office Communication Concerning Non-Compliance with Sequence Compliance Rules indicates that there are sequence identifiers missing from the subject application, including in the claims.

In response, applicants have amended the written description and the claims to include sequence identifiers as appropriate. A mark-up copy of the amendments to the written description is attached hereto as **Exhibit B**. A mark-up copy of the amendments to the claims is attached hereto as **Exhibit C**. Applicants have also amended the Sequence Listing to include sequences identified in the specification as originally filed which were not included in the Sequence Listing filed June 29, 2000 by applicants. Accordingly applicants also submit as **Exhibit D** hereto a paper copy Sequence Listing, a C.R.F Sequence Listing as **Exhibit E**, and a Statement in accordance with 37 C.F.R. §1.821(f) as **Exhibit F**. The amendments to the specification merely insert sequence ID numbers into the application. Applicants maintain that the amendments to the specification and Sequence Listing raise no issue of new matter. Accordingly, applicants respectfully request that this amendment be

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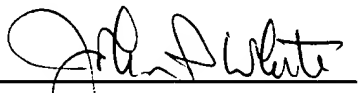
entered.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

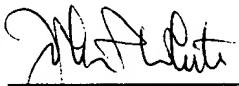
No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



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John P. White — Date
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1631
Box 1. Seq.

Docket No. 0575/50950/JPW/BJA

In re application of: Wayne A. Hendrickson et al.

Serial No.: 09/609,027 Examiner: Monika B. Sheinberg

Filed: June 29, 2000 Group Art Unit: 1631

For: CONJUGATED LIGANDS FOR THE STIMULATION OF BLOOD CELL PROLIFERATION BY EFFECTING DIMERIZATION OF RECEPTOR FOR STEM CELL FACTOR

February 4, 2002

HONORABLE ASSISTANT COMMISSIONER FOR PATENTS
Washington, D.C. 20231

S I R:

Transmitted herewith is an amendment to the above-identified application.

__X__ Small entity status of this application under 37 C.F.R. § 1.9 and § 1.27 has been established by a verified statement previously submitted.

_____ a verified statement to establish small entity status under 37 C.F.R. § 1.9 and § 1.27 is enclosed.

__X__ No additional fee is required.

The filing fee is calculated as follows:

	NUMBER AFTER AMEND-MENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		NUMBER OF EXTRA CLAIMS PRESENTED		RATE SMALL ENTITY	RATE OTHER ENTITY		FEE SMALL ENTITY	FEE OTHER ENTITY
Total Claims	47	-	* 47	=	*** 0	x	$9.00	$18.00	=	0	
Indepen-dent Claims	4	-	** 4	=	*** 0	x	$42.00	$84.00	=	0	
Multiple Dependent Claims(s) Presented For First Time:	____ Yes __X__ No						$140.00	$280.00		0	
							TOTAL ADDITIONAL FEE			$ 0	

*If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 20, write "20" in this space.

**If the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than 3, write "3" in this space.

***If the difference between the "NUMBER AFTER AMENDMENT" and the "HIGHEST NUMBER PREVIOUSLY PAID FOR" is less than "0", write "0" in the space.

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

1/18/2002
1 Mo: 2/18/2002
2 Mos: 3/18/2002
3 Mos: 4/18/2002
4 Mos: 5/18/2002
5 Mos: 6/18/2002
6 Mos: 7/18/2002
SMC

JAN 23 2002

EXAMINER	
ART UNIT	**PAPER**
	12

DATE MAILED:

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Commissioner of Patents and Trademarks

Non-Compliance with Sequence Compliance Rules.

It is reiterated that this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821 (a) (1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because there is a lack of sequence identifiers (SEQ ID NO: X) for the sequences refered to in the claims. It is noted that sequences which fall under the above sequence rules are present in the Figures and their amendments are acknowledged. However all sequences refered to within the specification are to have sequence identifiers. For example claim 15 refers to the polypeptide sequence of SCF and claim 21 points to specific residues of the sequence, yet no sequence identifier is presented. The sequences within the CFR are described to be a variety of stem cell factors thus the such claims as shown above can not be properly examined. Please provide a description of the sequences submitted. Applicant is required to complete the response within a time limit of one month from the date of this letter or as extended as follows.

Response to

The reply filed on 5 October 2001 is not fully responsive to the prior Office Action because of the following omission(s) or matter(s): the lack of sequence identifiers in the claims. See 37 CFR 1.111. Applicant is given ONE (1) MONTH or THIRTY (30) DAYS from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, can be reached on (703) 308-4028. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

November 21, 2001
Monika B. Sheinberg MBS

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

PTO-90C (Rev.3-98)

Applicants: Wayne A. Hendrickson et al
U.S. Serial No.: 09/609,027
Filed: June 29, 2000
Exhibit A

OIPE JC1
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Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/609,027	06/29/2000	Wayne A. Hendrickson	50950/JPW/EMW	1817

7590 01/18/2002

John P. White, Esq.
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER
SHEINBERG, MONIKA B

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/18/2002

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Mark-up Of Amendments to The Claims:

Additions to the text are indicated by underlining; deletions are indicated by square brackets.

Claim no. 6 has been amended as follows:

--6. The method of claim 5, wherein the receptor binding site comprises approximately amino acid residues 79-95 of the sequence shown in SEQ ID NO:1.--

Claim no. 15 has been amended as follows:

--15. A method for designing a compound capable of binding to (the) a stem cell factor (SCF) receptor site [of] comprising the steps of:

a) determining a binding site for the SCF receptor on the SCF based on the three-dimensional structure of SCF (SEQ ID NO:1) or an SCF polypeptide or portion/fragment thereof, atomic coordinates computed from X-ray diffraction data of a crystal comprising a polypeptide having an amino acid sequence portion of SCF capable of binding the receptor; and

b) designing a compound comprising an entity that binds the SCF receptor.--

Claim no. 21 has been amended as follows:

--21. The method of claim 20, wherein the (ooligopeptide) oligopeptide comprises a sequence, wherein functional moiety F_1 corresponds to a segment of amino acid residues from within N-terminal residues 1-10 of SCF (SEQ ID NO:1), functional moiety F_2 corresponds to a segment of amino acid residues from within residues 79-95 of SCF

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(SEQ ID NO:1), and functional moiety F_3 corresponds to a segment of amino acid residues located within three amino acid residues of amino acid residue 127 of (SEQ ID NO:1), wherein F_1, F_2, and F_3 are connected by connecting peptide [segements] segments X_n, X_m, and X_p, respectively, wherein n=0-5, m=0-5 and p=3-8 amino acid residues, respectively, and the conjugation moiety F_L is a cysteine residue.--

Claim no. 24 has been amended as follows:

--24. The method of claim 15, wherein an appropriate chemical scaffold of connecting segments has been designed to comprise (present) functional moieties F_1, F_2, and F_3, which have been selected by combinatorial chemistry for optimal receptor binding from a library of chemical moieties complementary to receptor-binding sites on the surface of SCF (SEQ ID NO:1).--

Claim no. 38 has been amended as follows:

--38. The method of claim 37, wherein the isolated SCF analog comprises amino acid residues of native or recombinant SCF1-165 (SEQ ID NO:22) or amino acid residues of a recombinant selenomethionyl SCF1-141 (SEQ ID NO:1).--

Claim no. 39 has been amended as follows:

--39. An isolated stem cell factor (SCF) molecule, which is an altered SCF, comprising any portion of amino acids 1-165 of a human SCF polypeptide (SEQ ID NO:1), optionally comprising an N-terminal methionine before amino acid residue 1, wherein the polypeptide has an amino acid sequence portion of SCF capable of binding to the SCF receptor.--

Claim no. 40 has been amended as follows:

--40. The altered isolated stem cell factor molecule of claim 39, wherein an alteration is selected from the group consisting of deletion, insertion and substitution of at least one amino acid residue from the naturally occurring amino acid sequence of SCF (SEQ ID NO:1).--

Claim no. 41 has been amended as follows:

--41. The altered isolated stem cell factor molecule of claim 40, wherein an alteration is a truncated SCF comprising amino acids 1-141 of a human SCF polypeptide (SEQ ID NO:1), optionally comprising an N-terminal methionine before amino acid residue 1.--

Claim no. 42 has been amended as follows:

--42. The altered isolated stem cell factor molecule of claim 40, wherein the substitution of at least one amino acid residue is selected from the group consisting of SCF(Y26C)(SEQ ID NO:11) disulfide-linked dimer, SCF(D25C)(SEQ ID NO:12), SCF(K62C)(SEQ ID NO:13), SCF(K78N,(SEQ ID NO:14); N81K (SEQ ID NO:15)), SCF(R117A,(SEQ ID NO:16);; I118A (SEQ ID NO:17)), SCF(E92A,(SEQ ID NO:18); S95A (SEQ ID NO:19)), and SCF(D124A, (SEQ ID NO:20); K127D (SEQ ID NO:21)).--

Claim no. 47 has been amended as follows:

--47. The altered isolated stem cell factor molecule of claim 46, wherein the change in said at least one amino acid residue from the naturally occurring amino acid residue(s) is selected from the group consisting of SCF(Y26C)(SEQ ID NO:11) disulfide-linked dimer,

SCF(D25C)(SEQ ID NO:12), SCF(K62C)(SEQ ID NO:13), SCF(K78N,(SEQ ID NO:14); N81K (SEQ ID NO:15)), SCF(R117A,(SEQ ID NO:16); I118A (SEQ ID NO:17)), SCF(E92A,(SEQ ID NO:18); S95A (SEQ ID NO:19)), and SCF(D124A, (SEQ ID NO:20); K127D (SEQ ID NO:21)).

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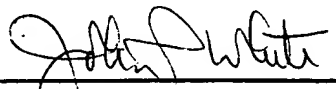
____ A check in the amount of $_____ is enclosed.

__X__ The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 03-3125 . Three copies of this sheet are enclosed.

__X__ Any filing fees under 37 C.F.R. §1.16 for the presentation of extra claims.

__X__ Any patent application processing fees under 37 C.F.R. §1.17.

Respectfully submitted,



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2/14/02

John P. White — Date
Reg. No. 28,678

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Mark-up Of Amendments to the Written Description

Additions to the text are indicated by underlining; deletions are indicated by square brackets.

The paragraph beginning page 4, line 5, has been amended as follows:

--SCF is expressed as membrane-associated forms of either 248 or 220 amino acid residues (Galli *et al.*, 1994, Lev et al., 1994, Besmer et al., 1997, Broudy, 1997). The two forms are a consequence of alternative mRNA splicing that includes or excludes exon 6. Exon 6 encodes a proteolytic cleavage site such that soluble SCF^{1-165} is released from the 248 amino-acid precursor. Residues 166-189 represent a tether to the membrane, residues 190-221 represent a hydrophobic transmembrane segment, and residues 222-248 represent a cytoplasmic domain. The 220 amino acid residue form lacks the cleavage site and tends to remain membrane-bound. Soluble SCF exists as a non-covalently associated dimer (Arakawa *et al.*, 1991). Each SCF monomer contains two intra-chain disulfide bridges, Cys4-Cys 89 and Cys43-Cys138 (Langley et al, 1992). The N-terminal 141 residues of SCF have been identified as a functional core, SCF^{1-141} (SEQ ID NO:1), that includes the dimer interface and portions that bind and activate the receptor Kit (Langley *et al.*, 1994).--

The paragraph beginning page 10, line 3, has been amended as follows:

--This invention provides a method for designing a compound (drug) capable of binding to the receptor of stem cell factor (SCF), Kit, comprising the steps of: a) determining a receptor binding site on the SCF based on the three dimensional structure of SCF (SEQ ID NO:1) or an SCF polypeptide capable of binding the receptor; and b)

designing a compound comprising an entity that binds the SCF receptor. Accordingly, the designed compound is an SCF ligand analog, since a portion or part of the compound, "the entity", mimics the portion of SCF that binds to the SCF receptor, Kit. In step (a), and infra, the receptor binding site may be determined from atomic coordinates computed from X-ray diffraction data of a crystal comprising a polypeptide having an amino acid sequence portion of SCF capable of binding the receptor.--

The paragraph beginning page 10, line 19, has been amended as follows:

--This invention provides a compound designed by the above-described method for designing a compound capable of binding to the receptor site of stem cell factor (SCF), Kit, comprising the steps of: a) determining a receptor binding site, on the SCF (SEQ ID NO:1) based on the atomic coordinates computed from X-ray diffraction data of a crystal comprising a polypeptide having an amino acid sequence portion of SCF capable of binding a ligand; and b) designing a compound comprising an entity that binds the SCF receptor. As used herein, the entity, i,.e. the portion, of the designed compound fits the ligand binding site on the SCF receptor.--

The paragraph beginning page 11, line 11, has been amended as follows:

--This invention provides an isolated stem cell factor (SCF) molecule, which is an altered SCF, comprising any portion of amino acids 1-165 of a human SCF polypeptide (SEQ ID NO:22), optionally comprising an N-terminal methionine before amino acid residue 1, wherein the polypeptide has an amino acid sequence portion of SCF capable of binding to the SCF receptor, Kit. Amino acid residue 1 of SCF is E, glutamic acid.--

The paragraph beginning page 20, line 11, has been amended as follows:

--Based on the correlation of structure to biological activity, one aspect of the present invention relates to SCF analogs. These analogs are molecules which have more, fewer, different or modified amino acid residues from the SCF amino acid sequence. The modifications may be by addition, substitution, or deletion of one or more amino acid residues. The modification may include the addition or substitution of analogs of the amino acids themselves, such as peptidomimetics or amino acids with altered moieties such as altered side groups. The SCF used as a basis for comparison may be of human, animal or recombinant nucleic acid-technology origin (although the working examples disclosed herein are based on the recombinant production of the 141 amino acid species of human SCF (SEQ ID NO:1), optionally having an extra N-terminal methionine residue). The analogs may possess functions different from natural human SCF molecule, or may exhibit the same functions, or varying degrees of the same functions. For example, the analogs may be designed to have a higher or lower biological activity, have a longer shelf-life or a decrease in stability, be easier to formulate, or more difficult to combine with other ingredients. The analogs may bind receptor but elicit no biological activity and may therefore be useful as an antagonist against SCF effect (as, for example, in the overproduction of SCF). From time to time herein the present analogs are referred to as proteins or peptides for convenience, but contemplated herein are other types of molecules, such as peptidomimetics or chemically modified peptides.--

Please replace the paragraph beginning page 33, line 3, has been amended as follows:

--In an embodiment of the above-described method the computer

expression allows for display of the amino acids of the SCF molecule. In another embodiment of the method the computer expression allows for display of each atom of the SCF molecule. In a further embodiment of the method the SCF molecule is a native or a selenomethionyl SCF. In another embodiment of the method the site on the SCF molecule for alteration is a receptor binding site on the surface of the SCF molecule. In a further embodiment of the method the receptor binding site comprises amino acid residues 79-85 (of SEQ ID NO:1). The SCF molecule may be a recombinant human SCF or a wild type naturally occurring human SCF. SCF wild type and recombinant may also be of other sources such as but not limited to rat or mouse. In an embodiment of the above-described method, the atomic coordinates of the crystal structure are set forth in Figure 8. In another embodiment the SCF analog comprises a polypeptide having an amino acid sequence portion of SCF capable of binding a receptor and having the overall three-dimensional conformation as shown in Figures 2A-2B, wherein the three-dimensional conformation is: a) anti-parallel, double-cross over 4-alpha helical bundle with a left hand twist; and b) overall dimensions of approximately 85 Å x 30 Å x 20 Å. In an embodiment the SCF analog comprises electron density distributions as set forth in Figures 1A, 1B, and 1C. In a further embodiment the SCF molecule is a native SCF or a selenomethionyl SCF.--

The paragraph beginning page 34, line 9, has been amended as follows:

--In another embodiment the receptor binding site comprises approximately amino acid residues 79-95 (of SEQ ID NO:1).--

The paragraph beginning page 34, line 29, has been amended as follows:

--This invention provides a composition comprising an isolated SCF

analog prepared according to the above-described method effective to treat a subject and a pharmaceutically acceptable carrier. In an embodiment of the composition, the isolated SCF analog has an alteration in at least one atom of the atomic coordinates of the crystal structure set forth in Figure 8. In another embodiment the isolated SCF analog comprises a polypeptide having an amino acid sequence portion of SCF capable of binding a receptor and having the overall three-dimensional conformation as shown in Figures 2A-2B, or an alteration thereof, wherein the three-dimensional conformation is: a) anti-parallel, double-cross over 4-alpha helical bundle with a left hand twist; and b) overall dimensions of approximately 85 Å x 30 Å x 20 Å. In a further embodiment the isolated SCF analog comprises electron density distributions as set forth in Figures 1A, 1B, and 1C. In an embodiment the isolated SCF analog comprises a native SCF1-165 (SEQ ID NO:22), a recombinant seleno-methionyl SCF1-141 (of SEQ ID NO:1), or a recombinant selenomethionyl SCF1-165 (of SEQ ID NO:22).--

The paragraph beginning page 35, line 24, has been amended as follows:

--In an embodiment of the composition the site on the isolated SCF molecule for alteration is a receptor binding site on the surface of the SCF molecule. In a further embodiment the receptor binding site comprises approximately amino acid residues 79-95 of SEQ ID NO:1.--

The paragraph beginning page 35, line 30, has been amended as follows:

--This invention provides a method of treating a subject having a disorder requiring SCF comprising administration of a composition comprising an isolated SCF analog prepared by the method of preparing a SCF analog or a compound designed by the method of

designing a compound capable of binding to the SCF receptor as described infra. In an embodiment the subject has a blood disorder. In another embodiment the disorder which the subject has is anemia, myeloproliferative disorder, neoplasia, nerve damage, infertility, intestinal damage, a pigmentation disorder, or immunodeficiency. In an embodiment the administration of the isolated SCF analog is for ex vivo or in vivro production of peripheral blood progenitors, ex vivo or in vivro stem cell expansion, ex vivo or in vitro growth of epithelial cells, ex vivo or in vitro growth of stromal cells, ex vivo or in vitro dendritic cell stimulation, and in vivo cell mobilization. In an embodiment the isolated SCF analog is administered orally or by any other routes described infra. In an embodiment the isolated SCF analog has an alteration in at least one atom of the atomic coordinates of the crystal structure set forth in Figure 8. In a further embodiment the isolated SCF analog comprises a native SCF1-165 (SEQ ID NO:22) or a recombinant selenomethionyl SCF1-141 (of SEQ ID NO:1). In another embodiment the site on the isolated SCF molecule for alteration is a receptor binding site on the surface of the SCF molecule. In a further embodiment the receptor binding site comprises approximately amino acid residues 79-95. In an embodiment the isolated SCF analog comprises a native or recombinant SCF1-165 (SEQ ID NO:22 or a recombinant selenomethionyl SCF1-141 (of SEQ ID NO:1). As used herein throughout SCF receptor is Kit.--

The paragraph beginning page 38, line 1, has been amended as follows:

--In an embodiment, the [ooligopeptide] oligopeptide comprises a sequence, wherein functional moiety F_1 corresponds to a segment of amino acid residues from within N-terminal residues 1-10 of SCF, functional moiety F_2 corresponds to a segment of amino acid residues from within residues 79-95 of SCF (SEQ ID NO:1), and

functional moiety F_3 corresponds to a segment of amino acid residues located within three amino acid residues of amino acid residue 127, wherein F_1, F_2, and F_3 are connected by connecting peptide [segements] segments X_n, X_m, and X_p, respectively, wherein n=0-5, m=0-5 and p=3-8 amino acid residues, respectively, and the conjugation moiety F_L is a cysteine residue.--

The paragraph beginning page 38, line 19, has been amended as follows:

--The amino acid residues located within 3 amino acid residues of amino acid residue 127 (SEQ ID NO:1) may be located within 3 residues in either direction of residue 127. In further embodiments the amino acid residues may be from 4 to 10 amino acid residues in either direction of amino acid residue 127.--

The paragraph beginning page 40, line 1, has been amended as follows:

--In another embodiment the [ooligopeptide] oligopeptide comprises a sequence, wherein functional moiety F_1 corresponds to a segment of amino acid residues from within N-terminal residues 1-10 of SCF (SEQ ID NO:1), functional moiety F_2 corresponds to a segment of amino acid residues from within residues 79-95 of SCF, and functional moiety F_3 corresponds to a segment of amino acid residues located within three amino acid residues of amino acid residue 127, wherein F_1, F_2, and F_3 are connected by connecting peptide segements X_n, X_m, and X_p, respectively, wherein n=0-5, m=0-5 and p=3-8 amino acid residues, respectively, and the conjugation moiety F_L is a cysteine residue. In a further embodiment the functional moieties F_1, F_2, and F_3 on the ligand heads have been selected by bacterial phage display for optimal receptor binding. In an embodiment the functional moieties and connecting peptide segments of an active oligopeptide ligand head are replaced by

chemical mimetics. In another embodiment an appropriate chemical scaffold of connecting segments has been designed to comprise (present) functional moieties F_1, F_2, and F_3, which have been selected by combinatorial chemistry for optimal receptor binding from a library of chemical moieties complementary to receptor-binding sites on the surface of SCF. In another embodiment the linker comprises an organic polymer having two ends capped at each end by a reactive capping moiety, F_c, which react covalently with the conjugation moiety, F_L, on the ligand head. In a further embodiment the organic polymer is polyethyleneglycol (PEG) comprising the structure $H[OCH_2CH_2]_nOH$, wherein n is 10-20. In another embodiment the capping moiety, F_c, is a thiol-reactive group such as N-ethyl maleimide. In an embodiment the conjugating moiety, F_L, is a thiol containing group such as cysteine.--

The paragraph beginning page 41, line 4, has been amended as follows:

--This invention provides a method of treating a subject comprising administration of a compound designed by the above described method. In an embodiment the subject has a blood disorder. In a further embodiment the blood disorder is anemia or immunodeficiency. In an embodiment the compound is administered orally or any other routes. In an embodiment the compound is an isolated SCF analog. In another embodiment the compound comprises an isolated SCF analog, whose alteration site is a receptor binding site on the surface of the altered SCF molecule. In another embodiment of the method the composition comprises a double-headed receptor SCF ligand analog having the structure set forth in Figure 10A. In an embodiment each ligand head of the double-headed SCF ligand analog is an oligopeptide having the structure set forth in Figure 10B. In another embodiment the ooligopeptide comprises a sequence, wherein functional moiety F_1 corresponds to a segment of amino acid residues from within N-terminal residues 1-10 of SCF,

functional moiety F_2 corresponds to a segment of amino acid residues from within residues 79-95 of SCF, and functional moiety F_3 corresponds to a segment of amino acid residues located within three amino acid residues of amino acid residue 127, wherein F_1, F_2, and F_3 are connected by connecting peptide segements X_n, X_m, and X_p, respectively, wherein n=0-5, m=0-5 and p=3-8 amino acid residues, respectively, and the conjugation moiety F_L is a cysteine residue. In a further embodiment the functional moieties F_1, F_2, and F_3 on the ligand heads have been selected by bacterial phage display for optimal receptor binding. In an embodiment the functional moieties and connecting peptide segments of an active oligopeptide ligand head are replaced by chemical mimetics. In another embodiment an appropriate chemical scaffold of connecting segments has been designed to comprise (present) functional moieties F_1, F_2, and F_3, which have been selected by combinatorial chemistry for optimal receptor binding from a library of chemical moieties complementary to receptor-binding sites on the surface of SCF. In another embodiment the linker comprises an organic polymer having two ends capped at each end by a reactive capping moiety, F_c, which react covalently with the conjugation moiety, F_L, on the ligand head. In a further embodiment the organic polymer is polyethyleneglycol (PEG) comprising the structure $H[OCH_2CH_2]_nOH$, wherein n is 10-20. In another embodiment the capping moiety, F_c, is a thiol-reactive group such as N-ethyl maleimide. In an embodiment the conjugating moiety, F_L, is a thiol containing group such as cysteine.--

The paragraph beginning page 44, line 20, has been amended as follows:

--This invention provides an isolated stem cell factor (SCF) molecule, which is an altered SCF, comprising any portion of amino acids 1-165 of a human SCF polypeptide (SEQ ID NO:7), optionally comprising an N-terminal methionine before amino acid residue 1, wherein the polypeptide has an amino acid sequence portion of SCF

capable of binding to the SCF receptor. In an embodiment of the altered isolated stem cell factor molecule an alteration is selected from the group consisting of deletion, insertion and substitution of at least one amino acid residue from the naturally occurring amino acid sequence of SCF.--

The paragraph beginning page 45, line 1, has been amended as follows:

--In a further embodiment an alteration is a truncated SCF comprising amino acids 1-141 of a human SCF polypeptide (SEQ ID NO:1), optionally comprising an N-terminal methionine before amino acid residue 1, E. In another embodiment the three-dimensional structure is altered from the atomic coordinates are set forth in Figure 8. In yet another embodiment the electron density distribution map is altered from the atomic coordinates are set forth in Figures 1A, 1B, or 1C. In a still further embodiment the substitution of at least one amino acid residue is selected from the group consisting of SCF(Y26C) (SEQ ID NO:11) disulfide-linked dimer, SCF(D25C) (SEQ ID NO:12), SCF(K62C), (SEQ ID NO:13); SCF(K78N (SEQ ID NO:14), N81K (SEQ ID NO:15)), SCF(R117A, (SEQ ID NO:16); I118A (SEQ ID NO:17)), SCF(E92A, (SEQ ID NO:18); S95A (SEQ ID NO:19)), and SCF(D124A, (SEQ ID NO:21); K127D (SEQ ID NO:22)). In another embodiment the overall three-dimensional conformation of the stem cell factor molecule has an altered three-dimensional structure of the αC-β2 loop.--

The paragraph beginning page 45, line 19, has been amended as follows:

--This invention provides a pharmaceutical composition comprising the above described altered isolated SCF molecule and a pharmaceutically acceptable carrier. In an embodiment the altered SCF molecule molecule is a hybrid molecule of the altered stem cell

factor molecule and a second protein or fragment thereof. As used herein, an SCF hybrid molecule is defined as a molecule wherein analog SCF is combined with with part or all of another protein such as another cytokine or another protein, which for example, effects signal transduction via entry through the cell through a SCF-SCF receptor transport mechanism. In an embodiment the alteration of the αC-β2 loop is a change in length of the amino acid sequence of the αC-β2 loop by a deletion or an insertion of at least one amino acid residue or a change in at least one amino acid residue from the naturally occurring amino acid residue(s) of the αC-β2 loop. In another embodiment the change in said at least one amino acid residue from the naturally occurring amino acid residue(s) is selected from the group consisting of SCF(Y26C) (SEQ ID NO:11) disulfide-linked dimer, SCF(D25C)(SEQ ID NO:12), SCF(K62C)(SEQ ID NO:13), SCF(K78N, (SEQ ID NO:14); N81K (SEQ ID NO:15)), SCF(R117A, (SEQ ID NO:16); I118A (SEQ ID NO:17)), SCF(E92A, (SEQ ID NO:18); S95A (SEQ ID NO:19)), and SCF(D124A, (SEQ ID NO:21); K127D (SEQ ID NO:22)).--

The paragraph beginning page 47, line 7, has been amended as follows:

--Human SCF^{1-141} (SEQ ID NO:1) was expressed recombinantly in *E. coli* as described previously (Langley *et al.*, 1994). For expression of SeMet SCF^{1-141}, the expression vector was transfected into the methionine auxotrophic *E. coli* strain FM5. Fermentation was carried out at 30°C in 8 liters of minimal medium consisting of ammonium sulfate (10 g/liter), glucose (5 g/liter), methionine (0.125 g/liter), phosphate salts, magnesium, citric acid, trace metals, and vitamins. When an OD_{600} of 3-5 was reached, a feed medium was added that consisted of the following components in a total volume of 1 liter: 100 g of ammonium sulfate, 450 g of glucose, 2 g of methionine, magnesium, trace metals, and vitamins. At an OD_{600} of 12.4, induction medium (one liter containing 100 g

of ammonium sulfate, 300 g of glucose, and 1 g of selenomethionine) was added and fermentation proceeded at 30°C. Five hours later (at an OD_{600} of approximately 16), the temperature was raised to 42°C to induce SCF expression and additional selenomethionine (1 g) was added. Cells were harvested 4 hours after the temperature shift (OD_{600} of approximately 16). SeMet SCF^{1-141} expression was estimated as 0.5 g/liter. Both SCF^{1-141} and $SeMetSCF^{1-141}$ were purified with minor modifications to previously described procedures (Langley et al., 1992, 1994). Both retain the initiating methionine (or SeMet) residue [position (-1)] (Langley et al., 1994). N-terminal amino acid sequencing was performed as described (Lu et al., 1991). About 90% SeMet was present in $SeMetSCF^{1-141}$ at each of the Met positions, based on amino acid analysis and N-terminal sequencing results (i.e. lack of recovery of Met residues for $SeMetSCF^{1-141}$ in comparison with SCF^{1-141}; data not shown).--

The paragraph beginning page 68, line 20, has been amended as follows:

--From studies of truncation and point mutants, Langley *et al* (1994) demonstrated that the N-terminal residues 1-4 and 1-10 and the Cys4-Cys89 disulfide bond are required for receptor binding and bioactivity, and that the Cys43-Cys138 disulfide bond and C-terminal residues past 127 are not required for receptor binding but may have some roles in cell proliferation activity. Moreover, alterations at Asn10 and Asn11 brought about by chemical isomerization or by mutagenesis have positive or negative effects depending on the substitution (Hsu *et al.*, 1998). A quadruple mutant of SCF (Arg121Asn, Asp124Asn, Lys127Asp and Asp128Lys) was found to be defective in bioactivity (Matous *et al.*, 1996). The molecular cause of this deficiency may be specific to Lys127 or due to indirect electrostatic effects. Arg121 and Asp124 are adjacent to the main N-linked glycosylation site, which is not involved in binding (see infra), and Asp128 is absent in the 1-127 truncation

mutant (SEQ ID NO:4) that retains full receptor-binding activity (Langley *et al.*, 1994). Moreover, a study of human-murine SCF chimeras narrowed the important receptor recognition epitopes to within residues 1 to 35 and 79 to 97 (Matous *et al.*, 1996), and the epitope of a neutralizing antibody was mapped to the region of residues 60-95 (Mendiaz et al., 1996) and 79-97 (Matous et al., 1996).--

The paragraph beginning page 77, line 3, has been amended as follows:

--Based on the X-ray crystallographic structure of SCF, several analogs were made and their biological activities were measured and compared to that of SCF wild type.

Analogs	Biological Activity (Approximate, compared to wild type SCF)
SCF(Y26C) disulfide linker (SEQ ID NO:11)	2 to 3 fold higher
SCF(D25C) (SEQ ID NO:12)	100 fold lower
SCF(K62C) (SEQ ID NO:13)	7 fold lower

These analogs were designed based on the structure of the dimer interface of SCF, which is a non-covalent dimer. Leu22, Pro23, Lys24, Asp25, Tyr26, Lys62 and Phe63 are in the dimer surface. The side chains of Leu22, Pro23, Tyr26, and Phe63 reside in the buried center of the dimerization site and are involved in hydrophobic interactions. The hydrophilic side chains of Lys24, Asp25 and Lys62 from each monomer residue in the solvent accessible surface, and are involved in ionic interactions. By replacing Tyr26 with Cys, [SCF(Y26C)], it was anticipated that a dimer covalently linked by a disulfide bond between the C26 residue of each monomer would form

because the distance between the β carbons of the two Cys26 rresidues would be less than 3Å.

Analogs	Biological Activity (Approximate, compared to wild type SCF)
SCF(K78N, N81K) (SEQ ID NO:14 & SEQ ID NO:15)	3 fold lower
SCF(R117A, I118A) (SEQ ID NO:16 & SEQ ID NO:17)	10 fold lower
SCF(E92A, S95A) (SEQ ID NO:19 & SEQ ID NO:20)	no change
SCF(D124A, K127D) (SEQ ID NO:21 & SEQ ID NO:22)	no change

These analogs were designed based on the assumption that there may be two distinct receptor binding sites, per monomer, as with growth hormone. One site would be on the face between helix A and helix C, and the other site would be on the face between helix A and helix D.--

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SEQUENCE LISTING

<110> HENDRICKSON, WAYNE
JIANG, XULIANG
LANGLEY, KEITH E
SYED, RASHID
ANN HSU, YUEH-RONG

<120> CONJUGATED LIGANDS FOR THE STIMULATION OF BLOOD CELL PROLIFERATION BY EF
FECTING
DIMERIZATION OF THE RECEPTOR FOR STEM CELL FACTOR

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35 40 45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65 70 75 80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
85 90 95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
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Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
        35                  40                  45

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
    50                  55                  60

Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
65                  70                  75                  80

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
                85                  90                  95

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
            100                 105                 110

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
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            20                  25                  30

Phe Ala Ala Ser Lys Asn Thr Thr Glu Lys Glu Thr Phe Cys Arg Ala
        35                  40                  45
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Ala Thr Val Leu Arg Gln Phe Tyr Ser His His Glu Lys Asp Thr Arg
50 55 60

Cys Leu Gly Ala Thr Ala Gln Gln Phe His Arg His Lys Gln Leu Ile
65 70 75 80

Arg Phe Leu Lys Arg Leu Asp Arg Asn Leu Trp Gly Leu Ala Gly Leu
85 90 95

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20 25 30

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35 40 45

Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln
50 55 60

Gly Leu Arg Gly Ser Leu Thr Lys Ile Lys Gly Pro Leu Thr Met Met
65 70 75 80

Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys
85 90 95

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100 105 110

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Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Tyr Met Pro Lys Lys
35 40 45

Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro
50 55 60

Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg
65 70 75 80

Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys
85 90 95

Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr
100 105 110

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Ser Thr Leu Thr
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35 40 45

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50 55 60

Val Glu Arg Leu Phe Lys Asn Leu Ser Leu Ile Lys Lys Tyr Ile Asp
65 70 75 80

Gly Gln Lys Lys Lys Cys Gly Glu Glu Arg Arg Arg Val Asn Gln Phe
85 90 95

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35 40 45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65 70 75 80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
85 90 95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
100 105 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
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Pro Pro Val Ala

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Val Ala Gly Met Asp Val Leu Pro Ser His Cys Trp Leu Arg Asp Met
35 40 45

Val Ile Gln Leu Ser Leu Ser Leu Thr Thr Leu Leu Asp Lys Phe Ser
50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Gly
65 70 75 80

Lys Ile Val Asp Asp Leu Val Leu Cys Met Glu Glu Asn Ala Pro Lys
85 90 95

Asn Ile Lys Glu Ser Pro Lys Arg Pro Glu Thr Arg Ser Phe Thr Pro
100 105 110

Glu Glu Phe Phe Ser Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
115 120 125

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Pro Pro Val Ala

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        35                  40                  45

Val Thr His Leu Ser Val Ser Leu Thr Thr Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Gly
65                  70                  75                  80

Lys Ile Val Asp Asp Leu Val Ala Cys Met Glu Glu Asn Ala Pro Lys
                85                  90                  95

Asn Val Lys Glu Ser Leu Lys Lys Pro Glu Thr Arg Asn Phe Thr Pro
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Glu Glu Phe Phe Ser Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
        115                 120                 125

Phe Met Val Ala Ser Asp Thr Ser Asp Cys Val Leu Ser Ser Thr Leu
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        35                  40                  45

Val Glu Gln Leu Ser Val Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
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50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65 70 75 80

Lys Ile Val Asp Asp Leu Val Glu Cys Thr Glu Gly Tyr Ser Phe Glu
85 90 95

Asn Val Lys Lys Ala Pro Lys Ser Pro Glu Leu Arg Leu Phe Thr Pro
100 105 110

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115 120 125

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Leu Pro Pro Val Ala
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35 40 45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65 70 75 80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
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Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
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Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
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Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Cys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

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Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Asn Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

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Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
50 55 60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65 70 75 80

Lys Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
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        35                  40                  45

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    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
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Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95
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Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ala Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser
    130                 135                 140
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<213> HOMO SAPIENS

<400> 18

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1               5                   10                  15

Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Ala Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser
    130                 135                 140
```

<210> 19
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<213> HOMO SAPIENS

<400> 19

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Glu Gly Ile Cys Arg Asn Arg Val Thr Asn Asn Val Lys Asp Val Thr
1               5                   10                  15
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Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ala Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser
    130                 135                 140
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Glu Gly Ile Cys Arg Asn Arg Val Thr Asn Asn Val Lys Asp Val Thr
1               5                   10                  15

Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95
```

```
Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Ala Ala Phe Lys Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser
    130                 135                 140
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1               5                   10                  15

Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Gln Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Asp Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser
    130                 135                 140
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<210> 22
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<213> HOMO SAPIENS

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Glu Gly Ile Cys Arg Asn Arg Val Thr Asn Asn Val Lys Asp Val Thr
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1               5                   10                  15

Lys Leu Val Ala Asn Leu Pro Lys Asp Tyr Met Ile Thr Leu Lys Tyr
            20                  25                  30

Val Pro Gly Met Asp Val Leu Pro Ser His Cys Trp Ile Ser Glu Met
        35                  40                  45

Val Val Gln Leu Ser Asp Ser Leu Thr Asp Leu Leu Asp Lys Phe Ser
    50                  55                  60

Asn Ile Ser Glu Gly Leu Ser Asn Tyr Ser Ile Ile Asp Lys Leu Val
65                  70                  75                  80

Asn Ile Val Asp Asp Leu Val Glu Cys Val Lys Glu Asn Ser Ser Lys
                85                  90                  95

Asp Leu Lys Lys Ser Phe Lys Ser Pro Glu Pro Arg Leu Phe Thr Pro
            100                 105                 110

Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp
        115                 120                 125

Phe Val Val Ala Ser Glu Thr Ser Asp Cys Val Val Ser Ser Thr Leu
    130                 135                 140

Ser Pro Glu Lys Asp Ser Arg Val Ser Val Thr Lys Pro Phe Met Leu
145                 150                 155                 160

Pro Pro Val Ala Ala
                165
```

Dkt. 0575/50950/JPW/BJA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Wayne A. Hendrickson et al.
U.S. Serial No.	:	09/609,027
Filed	:	June 29, 2000
For	:	CONJUGATED LIGANDS FOR THE STIMULATION OF BLOOD CELL PROLIFERATION BY EFFECTING DIMERIZATION OF THE RECEPTOR FOR STEM CELL FACTOR

OIPE JC1688 FEB 15 2002 PATENT & TRADEMARK OFFICE

1185 Avenue of the Americas
New York, New York 10036
February 4, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

STATEMENT IN ACCORDANCE WITH 37 C.F.R. §1.821(f)

In accordance with 37 C.F.R. §1.821(f), I hereby certify that the computer readable form containing the nucleic acid and/or amino acid sequences required by 37 C.F.R. §1.821(e) and submitted herewith in connection with the above-identified application contains the same information as the written "Sequence Listing" (16 pages) (Exhibit D) that is submitted herewith in connection with the above-identified application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

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